[0011] WO 2012/76942 A1 (Jun. 14, 2012)
[0012] KP 10-2090554 B1 (Mar. 12, 2020)

Non-Patent Document

[0013] Journal of the American Chemical Society, 1954, 76, 1182-1185
[0014] Journal of Medicinal Chemistry, 1986, 29, 1547-1550
[0015] Toxicology and Applied Pharmacology, 2018, 357, 39-49

DISCLOSURE

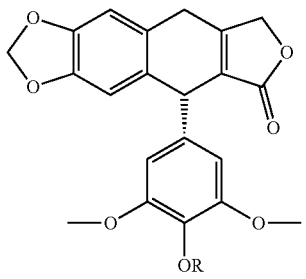
Technical Problem

[0016] As described above, many derivatives of podophyllotoxin have been studied for a new anticancer agent, but most of them were stopped the development stage due to efficacy and/or side effect. Thus, the present invention was extensively studied O-apopicropodophyllin derivatives to discover a new chemical entity, which is more potent and less side effect as compared with previous studies. Therefore, this present invention discloses a β-apopicropodophyllin derivative, stereoisomer, useful of as an anticancer agent, pharmaceutically acceptable salt, and a preparation method of the derivative.

Technical Solution

[0017] The compound of Formula 1 according to the present invention is a β-apopicropodophyllin derivative accomplished by modification of 4'-position of β-apopicropodophyllin:

[Formula 1]



[0018] In Formula 1, R is a C_2 to C_{10} alkyl group, a C_2 to C_{10} alkyl group containing an allyl- or alkyne, a —$[CH_2]_n$—C_3 to C_8 cycloalkyl group, a substituted or unsubstituted —$[CH_2]_n$-phenyl group, a substituted or unsubstituted —$[CH_2]_n$—C_5 to C_6 heteroaromatic group, a —C(═O)—C_1 to C_8 alkyl group, a substituted or unsubstituted —C(═O)—$[CH_2]_n$-phenyl group, or a substituted or unsubstituted —C(═O)—$[CH_2]_n$—C_5 to C_6 heteroaromatic group, wherein n is an integer of 0 to 6.

[0019] A method of preparing a compound of Formula 1 comprises a step obtaining a target compound by reacting 4'-demethyl-β-apopicropodophyllin[(5S)-5-(4-hydroxy-3,5-dimethoxy-phenyl)-5,9-dihydro-8H-furo[3',4':6,7]naphtho [2,3-d][1,3]dioxol-6-one] with a chemical (R-L) in which a leaving group (L) binds to a substituent (R) introduced to the 4'-position of 4'-demethyl-β-apopicropodophyllin in the presence of an organic or inorganic base.

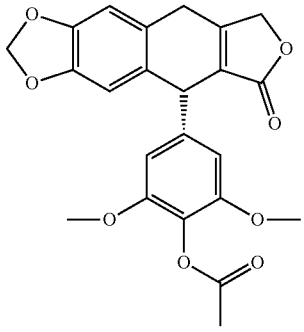
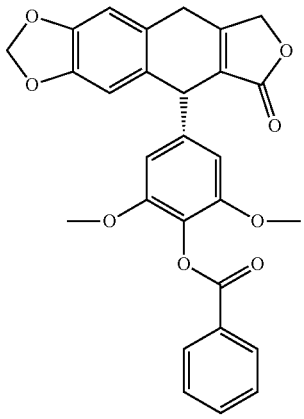
Advantageous Effects

[0020] The compound of Formula 1 of the present invention exhibits a potent anticancer effect in selected human cancer cell lines i.e., lung, colon, and blood cancer cell line. Accordingly, the compound of Formula 1 can be usefully used as a new anticancer agent that can replace the conventional podophyllotoxin derivatives.

Modes of the Invention

[0021] Preferred compounds among the Formula 1 compounds according to the present invention are shown in the following [Table 1].

TABLE 1

No.	chemical structure
1-1	
1-2	
1-3